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Merkel cell carcinoma in pelvic lymph nodes after surgical staging for endometrial cancer: A case report and review of the literature

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ABSTRACT

INTRODUCTION: Merkel cell carcinoma (MCC) is a rare malignant neuroendocrine tumor of the skin.
PRESENTATION OF CASE: We present a case of MCC in pelvic lymph nodes, revealed after surgical staging for endometrial cancer. A 54-year-old Caucasian woman presented to our department with a three-month history of postmenopausal bleeding. After proper preoperative evaluation, the patient underwent total abdominal hysterectomy, bilateral salpingo-ophorectomy and pelvic lymph node dissection. The pathology report confirmed the presence of a small, grade I, endometrioid adenocarcinoma and MCC in the pelvic lymph nodes. Primary site of the disease could not been retrieved. The tumor board decided adjuvant chemotherapy (carboplatin and etoposide) and close follow-up every 2 months. Our patient is alive with no evidence of disease 12 months after surgery.
DISCUSSION: It is noteworthy that 19% of the patients with MCC had lymph node metastasis with no apparent primary lesion. The mechanism of this regression remains unclear, although a higher apoptotic activity has been observed in MCC than other skin tumors. In addition, other co-malignancies have also been linked to MCC patients. The explanation for the frequent occurrence of other primary neoplasms in patients with MCC is still unclear. However, a reasonable cause could be an altered genetic profile or an immuno-compromised situation in these patients.
CONCLUSION: Further analytic investigations are needed to clarify the role of various factors in the spontaneous regression or not of this neuroendocrine tumor as well as in the simultaneous genesis of other primary carcinomas.

1. Introduction

Merkel cell carcinoma (MCC) is a rare malignant neuroendocrine tumor of the skin, first described by Toker in 1972 as "trabecular carcinoma".[1] It mainly affects elderly Caucasians, presenting at an average age of 69 years with immunosuppressed patients being the most susceptible to the disease.[2] Sun-exposed areas of the skin as well as lower extremities appear to be most frequently involved. Local recurrences and dissemination to regional lymph nodes and distant organs (liver, lung, bones) are characteristics of this aggressive tumor.[2]

However, rare cases of MCC confined to a lymph node without an apparent primary site have been reported.[3–7] It has been proposed that MCC originates from immature totipotent stem cells that acquire neuroendocrine characteristics upon malignant transformation.[6] The occasional presence of squamous or eccrine differentiation in these tumors also suggests stem cell origin.[8]

Herein, we present a case of MCC in pelvic lymph nodes, revealed after surgical staging for endometrial cancer. To our knowledge, pelvic nodal involvement has never been reported in literature as a clinical presentation of the disease.

2. Case presentation

A 54-year-old Caucasian woman presented to our department with a three-month history of postmenopausal bleeding. Her medical history was unremarkable while her obstetrical included 2 uncomplicated full-term vaginal deliveries and one first trimester miscarriage.

Pelvic examination revealed normal size uterus and adnexae, without significant bleeding through the external cervical os. Transvaginal ultrasound showed an endometrial thickness of 12 mm. Dilatation and curettage followed and histology disclosed a well-differentiated endometrioid adenocarcinoma of the uterus. After proper preoperative evaluation, our patient underwent thorough surgical staging including total abdominal hysterectomy, bilateral salpingo-ophorectomy and pelvic lymph node dissection.

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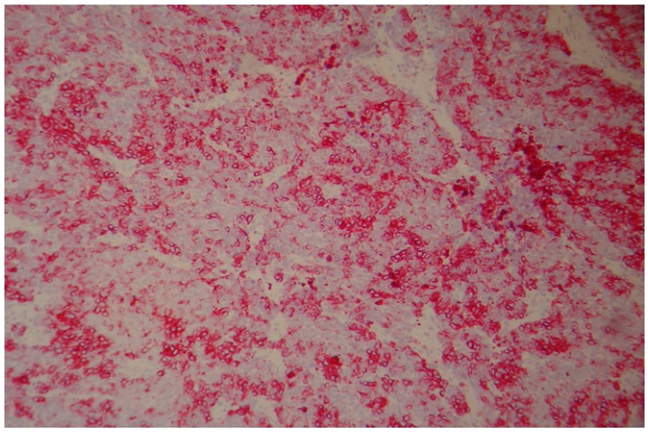

Fig. 1. Positive immunohistochemical staining for cytokeratin 20.

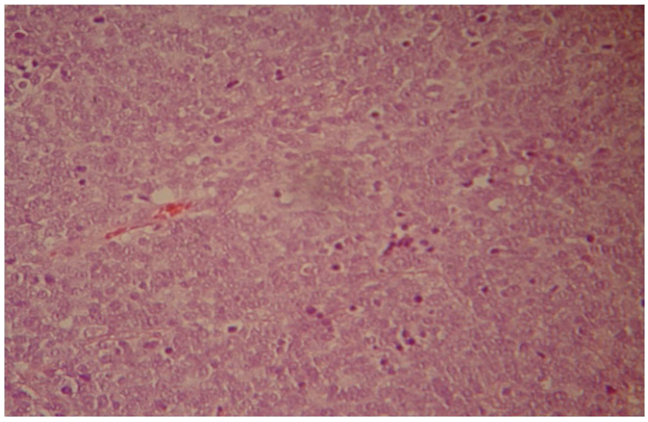

Fig. 2. Scant eosinophilic cytoplasm, round nuclei and multiple nucleoli on HE.

The pathology report confirmed the presence of a small, grade I, endometrioid adenocarcinoma with superficial invasion of the myometrium and no extension to the cervix. A block of lymph nodes from the right parametrium were filled with multiple solid, small monomorphic tumor cells with large, oval, pale nuclei. Dispersed chromatin, scanty cytoplasm and multiple nucleoli were present. Lymph nodes from the left parametrium were negative for pathological findings. Immunohistochemical stains were positive for CK20 (Figs. 1 and 2) in a dot-like perinuclear pattern, synaptophysin (Fig. 3) and pankeratin and negative for LCA, Bcl-2, CD3, CD20, CK7, Vimentin, CD99 and CK5/6. In addition, S-100, HMB-45 and TTF-1 were also not expressed, excluding the possibility of certain metastasis (melanoma, thyroid, lung, brain). With such a staining profile, a diagnosis of MCC in pelvic lymph nodes was assumed.

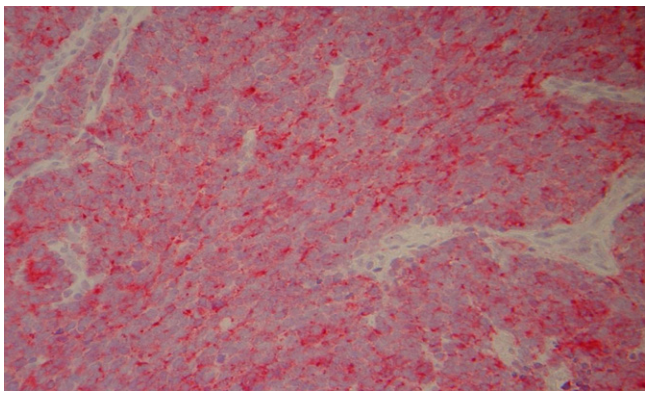

Fig. 3. Tumor cells are positive for synaptophysin.

Abdominal computed tomography of the chest and abdomen performed in our patient after surgery, as well as evaluation by a consultant dermatologist could not reveal primary site of the disease. The tumor board decided that adjuvant chemotherapy (carboplatin and etoposide) and close follow-up every 2 months was the correct course of action. Our patient is alive with no evidence of disease 12 months after surgery.

3. Discussion

MCC is an uncommon tumor with an annual incidence of approximately 0.2–0.45 cases per 100,000 inhabitants.[9] In a review of 661 cases conducted in 2000, 2% presented with an unknown primary site.[10] However, in a later series from Australia, 19% of the patients with MCC had lymph node metastasis with no apparent primary lesion.[11]

Hypotheses that have been proposed to explain the existence of an epithelial tumor confined to a lymph node are: (a) malignant transformation of a pre-existing intranodal epithelial nest, (b) spread from a primary tumor that regressed after metastasis to the node and (c) origin from a subset of lymphoreticular cells which share cytokeratin pattern and endocrine features with epithelial cells.[12] It is still unclear to us whether our case represents a primary or metastatic MCC.Primary tumors, most often of the skin (squamous and basal cell carcinoma) as well as hematological malignancies (non-Hodgkin lymphoma) have been associated with MCC patients.[13–15] Adenocarcinomas of the breast and ovaries have also been linked to the disease. Endometrial cancer has not been related to MCC and pelvic nodal involvement as part of this rare neoplasm has never been reported in literature.It is noteworthy that all co-malignancies, whether they appear before, after or simultaneously with MCC, behave more aggressively.[16,17] The explanation for the frequent occurrence of other primary neoplasms in patients with MCC is still unclear. However, a reasonable cause could be an altered genetic profile or an immuno-compromised situation in these patients.[18] Our patient has been free of disease for 12 months; close follow-up (evaluation by a dermatologist every 2 months and CT scans every 6 months) has not revealed primary site or recurrence.

Considering the reported incidence of MCC, the estimated rate of spontaneous regression is higher than expected (1.7–3%).[19] The mechanism of this regression remains unclear, although a higher apoptotic activity has been observed in MCC than other skin tumors. It has been suggested that T-cell related cytokines such as interferons have a leading role in the spontaneous regression of neuroendocrine tumors.[20] We truly hope that this will be the scenario for our patient.

4. Conclusion

In conclusion it can be said that MCC represents a diagnostic dilemma with difficult therapeutic criteria. Further analytic investigations are needed to clarify the role of various factors in the spontaneous regression or not of this neuroendocrine tumor as well as in the simultaneous genesis of other primary carcinomas. Because of its rare incidence and variable clinical presentations, a multidisciplinary approach is usually of crucial importance in establishing management guidelines.

Conflict of interest statement

The authors declare that potential conflicts of interest do not exist.

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None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Nikolaos Thomakos: Writing the manuscript, study design.
Dimitrios Zacharakis: Writing the manuscript, study design.
Nikolaos Akrivos: Writing the manuscript.
Flora Zagouri: Pathology report responsible.
Maria Simou: Data collection, pub-med search.
Aristotle Bamias: Tumor board member, pub-med search.
Meletios-Athanassios Dimopoulos: Responsible of chemotherapy treatment, Reviewing the manuscript.
Alexandros Rodolakis: Reviewing the manuscript, Surgeon of the patient.
Aris Antsaklis: Reviewing the manuscript, Surgeon of the patient.

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